Docket No.: CytRx/012 US (004049-0018-101)
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Greensmith et al.

Application No.: 10/582,124 | Confirmation No.: 1776

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For: USE OF HYDROXIMIC ACID HALIDE DERIVATIVE IN THE TREATMENT OF NEURODEGENERATIVE DISEASES | Examiner: Christopher R. Stone

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 35 U.S.C. § 1.132 OF LINDA GREENSMITH

Sir:

I, Linda Greensmith, of 84 Bedford Avenue, Barnet, Hertfordshire, EN5 2ET, UK, hereby declare as follows:

1. I am currently a Professor of Neuroscience and The Graham Watts Senior Research Fellow in the Sobell Department of Motor Neuroscience and Movement Disorders of the University College of London Institute of Neurology in London, England. I have been a Professor at University College of London since 2009. Prior to this, I held the position of Reader In Neuroscience at UCL. I received a BSc. in Physiology from University College London in 1984 and a Ph.D. in Neuroscience from University College London in 1989.

2. Attached herewith as Exhibit A is my current *curriculum vitae*.

3. I am the lead author of and the principle investigator in the scientific paper entitled "Upregulation of Heat Shock Proteins Rescues Motoneurones from Axotomy-Induced Cell Death in Neonatal Rats" which was published in the peer-reviewed journal *Experimental Neurology* in volume 176 on pages 87-97 in 2002 ("the Kalmar paper"). I

am thoroughly familiar with the contents of the Kalmar paper and all the experimental materials and methods recited therein.

4. The Kalmar paper describes the use of the chemical compound BRX-220 in various experiments. The Kalmar paper does not disclose the chemical structure or identity of BRX-220.

5. At the priority date of the present patent application, and at the time of publication of the Kalmar paper, BRX-220 was a proprietary compound which was not available to the public. Additionally, at the priority date of the present patent application and at the time of publication of the Kalmar paper, the chemical structure of BRX-220 was also proprietary and neither known by nor available to the public.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title XVIII of the United States Code and that willful false statements may jeopardize the validity of this Application for Patent or any patent issuing thereon.

Linda Greensmith

Linda Greensmith

Dated: January 27, 2010 Signature: _____

EXHIBIT A

Curriculum Vitae

LINDA GREENSMITH

Personal Details

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London WC1N 3BG
UK

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Current Position: Professor of Neuroscience

Education/Qualifications

1981-1984	BSc Physiology, University College London
1984-1985	Postgraduate Diploma in Immunology, London University
1986-1989	PhD Neuroscience, University College London

Professional History

1989-1991	Science and Engineering Research Council Postdoctoral Fellowship Department of Anatomy and Developmental Biology, UCL
1991-1992	Postdoctoral Research Assistant Department of Anatomy, Charing Cross and Westminster Medical School
1992-1994	Postdoctoral Research Fellow St. Mary's Hospital Medical School, Imperial College London
1994-1996	Senior Research Fellow Department of Anatomy and Developmental Biology, UCL
1996-1999	Wellcome Trust Advanced Training Fellowship University College London Medical School
1999-2005	Graham Watts Senior Research Fellow - Lecturer UCL Institute of Neurology
2005- Present	Reader in Neuroscience, UCL Institute of Neurology
2005- Present	Deputy Head of Department, Sobell Department of Motor Neuroscience and Movement Disorders, IoN
2009- Present	Professor of Neuroscience, UCL Institute of Neurology

Summary of Grant Income:

Grants awarded prior to appointment at ION between 1986-1999: approx. £560,000
Grants awarded and completed between 1999-2008: approx. £1.8 million
Active awards: 2004-present: 13 awards with income of approximately £5.5 million (including 3 Programme Grants, 1 as sole investigator)

Graduate Student Supervision 1999-present:

Primary supervisor of 15 PhD students
Secondary supervisor of 5 PhD students
Primary supervisor of 11 MSc students

Editorial Board Membership

2008 - present The Amyotrophic Lateral Sclerosis Journal
2009 - present European Journal of Neuroscience; Section Editor: Molecular and Developmental Neuroscience

Research/Scientific Advisory Positions

2005 - 2009	Motor Neuron Disease Association UK, Research Advisory Panel Member
2005 - present	Muscular Dystrophy Association USA, Ad hoc Review Committee
2005 - present	Scientific Advisory Board CyTrx Corporation, Los Angeles USA
2007 - 2008	Program Committee Member - 19th International Symposium on ALS/MND; Co-Chair Basic Science Sessions
2008	Royal Irish Academy – Irish Research Council for Science, Engineering and Technology Fellowship Assessment Committee, Ireland
2008-present	The Thierry Latran Foundation for ALS Research – Founder Member and Scientific Research Advisory Committee member of new European ALS Research Foundation
2008	Muscular Dystrophy Association USA, Translational Research Infrastructure Grant Ad Hoc Review Committee
November 2008	International Scientific Review Committee - Genoma España, Foundation
Sept 2009-present	Agency for Research on Amyotrophic Lateral Sclerosis - Italy, International Scientific Committee

Publications (since 2004)

DM Kieran, B Kalmar, JRT Dick, J Riddoch-Contreras, G Burnstock & L Greensmith (2004). Treatment with arimoclomol, a coinducer of heat shock proteins, delays disease progression in ALS mice **Nature Medicine** 10, 402-405.

J Dekkers, P Bayley, JRT Dick, B Schwaller, MW Berchtold & L Greensmith. (2004) Overexpression of parvalbumin in transgenic mice rescues motoneurons from injury-induced cell death. **Neuroscience** 123, 459-466.

D Kieran & L Greensmith (2004) Inhibition of calpains, by treatment with leupeptin, improves motoneuron survival and muscle function in models of motoneuron degeneration. **Neuroscience** 125, 427-439.

P S Sharp, JRT Dick and L Greensmith (2005) The effect of peripheral nerve injury on disease progression in the SOD1 (G93A) mouse model of ALS. **Neuroscience** 130, 897-910.

GS Ralph, PA Radcliffe, DM Day, JM Carthy, MA Leroux, DCP Lee, L-F Wong, LG Bilsland, L Greensmith, SM Kingsman, KA Mitrophanous, ND Mazarakis and M Azzouz (2005) Silencing of mutant SOD1 using interfering RNA induces long term reversal of ALS in a transgenic mouse model. **Nature Medicine** 11, 429-433.

F Achilli, S Boyle, D Kieran, R Chia, M Hafezparast, J E Martin, G Schiavo, L Greensmith, W Bickmore and EMC Fisher (2005) The SOD1 transgene in the G93A mouse model of amyotrophic lateral sclerosis lies on distal mouse chromosome 12. **Amyotrophic Lateral Sclerosis and Other Motor Neuron Disorders** 6, 111-114.

DM Kieran, M Hafezparast, S Bohnert, JRT Dick, G Schaivo, J Martin, E Fisher & L Greensmith (2005) Mutations in Dynein delay disease progression in $SOD1^{(G93A)}$ transgenic mice, a model of ALS. **Journal of Cell Biology** 169, 561-567.

B Kalmar, D Kieran and L Greensmith (2005) Molecular chaperones as therapeutic targets in amyotrophic lateral sclerosis. **Biochemical Society Transactions** 33, 551-552.

N. Nirmalananthan & L. Greensmith (2005) Amyotrophic Lateral Sclerosis – Recent advances and future therapies. **Current Opinion in Neurology** 18, 712-719.

L G Bilsland, JRT Dick, G Pryce, S. Petrosino, V Di Marzo, D Baker & L Greensmith (2006) The neuroprotective effects of cannabinoids in the $SOD1^{G93A}$ mouse model of ALS. **FASEB Journal** 20, 1003-1005.

DD Ateh, IK Hussain, AH Mustafa, KM Price, R Gulati, CD Nickols, MM. Bird, L Greensmith, M Hafezparast, EMC Fisher, CS. Baker & JE Martin (2008) Dynein–dynactin complex subunits are differentially localized in brain and spinal cord, with selective involvement in pathological features of neurodegenerative disease. **Neuropathology and Applied Neurobiology**, 34, 88–94

B Kalmar & L Greensmith (2008) Heat shock proteins as therapeutic targets in ALS in Heat Shock Proteins and The Brain: Implications for Neurodegenerative Diseases and Neuroprotection: Section 1- Heat shock proteins and neurodegenerative diseases. Edited by I.R Brown (Springer)

LG Bilsland and L Greensmith (2008) The Endocannabinoid System in Amyotrophic Lateral Sclerosis in The Endocannabinoid System in Neuroinflammatory Diseases, **Current Pharmaceutical Design**. 14, 2306-2316.

B Kalmar, S Novoselov, A Gray, ME Cheetham, B Margulis and L Greensmith (2008) Late stage treatment with Arimoclomol delays disease progression and prevents protein aggregation in the SOD1 mouse model of ALS. **Journal of Neurochemistry** 107, 339-350

LG Bilsland, N Nirmalananthan, J Yip, L Greensmith & MR Duchen (2008) Expression of mutant $SOD1^{G93A}$ in astrocytes induces functional deficits in motoneuron mitochondria. **Journal of Neurochemistry**. 107, 1271-1283

J Riddoch-Contreras, S-Y Yang, JRT Dick, G Goldspink, RW Orrell & L Greensmith (2008) Mechano-Growth Factor, an IGF-I splice variant, rescues motoneurons and improves muscle function in $SOD1^{G93A}$ mice. **Experimental Neurology** 215, 281–289

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D Boërio, L Greensmith and H Bostock (2009) Excitability properties of motor axons in the maturing mouse **Journal of the Peripheral Nervous System** 14(1):45-53

B Kalmar and L Greensmith (2009) Induction of heat shock proteins for protection against oxidative stress in "Controlling Oxidative Stress- therapeutic and delivery strategies. **Advanced Drug Delivery Reviews** 61, 310–318.

F Achilli, V Bros-Facer, HP Williams, GT Banks, M AlQatari, R Chia, V Tucci, M Groves, CD Nickols, KL Seburn, R Kendall, MZ Cader, K Talbot, J van Minnen, RW Burgess, S Brandner, JE Martin, M Koltzenburg, L Greensmith, PM Nolan and EMC Fisher (2009) A novel mouse model with a point mutation in glycyl-tRNA synthetase (*GARS*) has axonal loss and profoundly reduced enzyme activity in homozygotes. **Disease Models and Mechanisms** 2 (7-8), 359-373

GT Banks, V Bros-Facer, HP Williams, R Chia, F Achilli, J Barney Bryson, L Greensmith and EMC Fisher (2009) Mutant glycyl-tRNA synthetase ameliorates the $SOD1^{G93A}$ motor neuron degeneration phenotype but does not greatly affect mice with a mutation in the dynein heavy chain gene. **PLOS One** 4(7):e6218.

F Mackenzie, R Romero, F Wong, D Williams, T Gillingwater, H Hilton, J Dick, J Riddoch-Contreras, L Ireson, N Powles-Glover, P Underhill, T Hough, R Arkell, L Greensmith, R Ribchester & G Blanco (2009) The TRPP protein PKD1L2 is a regulator of neuromuscular homeostasis. **Human Molecular Genetics** 18(19):3553-66.

D Boërio, B Kalmar, L Greensmith and H. Bostock (2009) Changes in excitability of mouse motor axons in the mutant $SOD1^{G93A}$ model of amyotrophic lateral sclerosis. **Muscle and Nerve** In press